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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/564,070	03/03/2006	Sutisak Kitareewan	DC0266US.NP	5026

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LICATA & TYRRELL P.C.
66 E. MAIN STREET
MARLTON, NJ 08053

EXAMINER	
MARTIN, PAUL C	
ART UNIT	PAPER NUMBER
1657	

NOTIFICATION DATE	DELIVERY MODE
09/07/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

poreilly@licataandtyrrell.com

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/564,070	**Applicant(s)** KITAREEWAN ET AL.	
	Examiner PAUL C. MARTIN	**Art Unit** 1657	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 23 August 2010 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *4* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *8*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attached.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/Rebecca E. Prouty/
Primary Examiner, Art Unit 1652

DETAILED ACTION

Claim 8 is pending in this application and was examined on its merits.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 8 remains rejected under 35 U.S.C. § 103(a) as being unpatentable over Yoshida et al. (1996) in view of Bard et al. (1977) for reasons of record set forth in the prior action.

Response to Arguments

Applicant's arguments filed 08/23/2010 have been fully considered but they are not persuasive.

The Applicant argues that the cited passage in Yoshida et al. teaches that "ATRA accelerates the degradation of PML-RARα in the proteasome pathway", in contrast to the instant invention which is directed to the identification of agents that induce the lysosome-dependent degradative pathway and that the instant assay requires the identification of agents that both destabilize lysosomes and increase PML-RARα (Remarks, Pg. 5, Lines 11-25 and Pg. 6, Lines 1-12).

This is not found to be persuasive for the following reasons, as discussed in the prior action, the claims are drawn to a method comprising (preamble/step ii) contacting a cell that expresses PML/RARα with an agent and detecting whether said agent increases PML/RARα degradation and contacting a cell that expresses PML/RARα with an agent and detecting whether said agent destabilizes lysosomes of the cell, as determined by vital staining of lysosomes or release of lysosomal proteins into the cytosol (preamble and step i). Yoshida et al. teaches a method of identifying an agent that increases oncogenic protein degradation comprising contacting an APL (acute promyelocytic leukemia) cell that expresses PML/RARα with the anti-cancer agent ATRA (all-trans-retinoic acid) and detecting whether ATRA increases PML/RARa protein degradation. Yoshida et al. does not teach a method for identifying an agent which destabilizes lysosomes comprising contacting a cell that expresses PML/RARa with an agent and detecting whether the agent destabilizes lysosomes of the cell as determined by vital staining of lysosomes or release of lysosomal proteins into the cytosol.
Bard et al. teaches a method wherein cartilage cells are contacted with known
anticancer retinoid compounds and detecting whether the retinoids destabilize
lysosomes as determined by the release of lysosomal proteins into the cytosol and the
resulting degradation of the cartilage matrix as a measure of toxicity. It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the method of Yoshida et al. for identifying an anti-cancer agent that increases oncogenic protein degradation with the method of Bard et al. for identifying an anti-cancer agent which destabilizes lysosomes because it is prima facie obvious to combine two methods, each taught separately as useful for screening the
same anti cancer agent (retinoic acid) in order to form a single combined assay for
detecting an anti-cancer agent which both destabilizes lysosomes and increases
PML/RARα degradation. The MPEP states:
"It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be
used for the very same purpose ....
[T]he idea of combining them flows logically from their
having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846,850, 205 USPQ 1069, 1072 (CCPA 1980)

The Applicant argues that the whole of the teachings of Yoshida et al. show that PML/RARα is degraded by the proteosomal pathway, i.e., a non-lysosomal pathway. Therefore, Applicant asserts that the reference teaches away from doing what Applicant has done, determining whether an agent destabilizes lysosomes and increases lysosomal-dependent PML/RARα protein degradation and that there would be no motivation to look to the teachings of Bard et al. for determining whether an agent destabilizes lysosomes (Remarks, Pg. 6, Lines 19-27).
This is not found to be persuasive for the following reasons, in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., determining whether an agent increases lysosomal-dependent PML/RARα protein degradation) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Whatever pathway of degradation taught by Yoshida et al., the claims only require two steps. Yoshida et al. taught limitations found in the preamble and step ii, while Bard et al. was brought in for its teachings related to step i. Both methods were drawn to screening for the same class of compounds, anti-cancer retinoids. Therefore, it is prima facie obvious to combine the two methods into a single screening method.

The Applicant argues that the Advisory action of 08/09/2010 asserts that one of ordinary skill in the art would recognize that if lysosomes were destabilized by ATRA, the degradation of aberrant proteins would have to proceed by another route, such as the non-lysosomal ubiquitin-proteosomal pathway, however Applicant's assert that the teachings of Bard et al. cannot be considered as pertinent to the teachings of Yoshida et al. as Bard et al. teaches that retinoids are toxic at higher than physiological concentrations while Yoshida et al. do not discuss the toxicity of ATRA in a method of differentiation of APL cells (Remarks, Pg. 6, Lines 28-31 and Pg. 7, Lines 1-14).

This is not found to be persuasive for the following reasons, in response to applicant's argument that the references are directed to different methods utilizing retinoid compounds at different concentrations, the fact remains that in combination the two references meet the limitations of claim 8 and prima facie reasoning exists as to why such a combination would be obvious as discussed in the prior actions and above.

No Claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL C. MARTIN whose telephone number is (571)272-3348. The examiner can normally be reached on M-F 12pm-8pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Paul Martin
Examiner
Art Unit 1657

08/31/2010